

Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
 1 5 10 15
 Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
 20 25 30
 Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
 35 40 45
 Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
 50 55 60
 Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
 65 70 75 80
 Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
 85 90 95
 Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
 100 105 110
 Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
 115 120 125
 Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr
 130 135 140
 Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
 145 150 155 160
 Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
 165 170 175
 Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
 180 185 190
 Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
 195 200 205
 Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
 210 215 220
 Ser Leu Ser Leu Ser Pro Gly Lys
 225 230

FIGURE 1

Met 1	Asn	Lys	Trp	Leu 5	Cys	Cys	Ala	Leu	Leu 10	Val	Leu	Leu	Asp	Ile 15	Ile
Glu	Trp	Thr	Thr 20	Gln	Glu	Thr	Leu	Pro 25	Pro	Lys	Tyr	Leu	His 30	Tyr	Asp
Pro	Glu	Thr 35	Gly	His	Gln	Leu	Leu 40	Cys	Asp	Lys	Cys	Ala 45	Pro	Gly	Thr
Tyr	Leu 50	Lys	Gln	His	Cys	Thr 55	Val	Arg	Arg	Lys	Thr 60	Leu	Cys	Val	Pro
Cys 65	Pro	Asp	His	Ser	Tyr 70	Thr	Asp	Ser	Trp	His 75	Thr	Ser	Asp	Glu	Cys 80
Val	Tyr	Cys	Ser	Pro 85	Val	Cys	Lys	Glu	Leu 90	Gln	Ser	Val	Lys	Gln 95	Glu
Cys	Asn	Arg	Thr 100	His	Asn	Arg	Val	Cys 105	Glu	Cys	Glu	Glu	Gly 110	Arg	Tyr
Leu	Glu	Ile 115	Glu	Phe	Cys	Leu	Lys 120	His	Arg	Ser	Cys	Pro 125	Pro	Gly	Ser
Gly	Val 130	Val	Gln	Ala	Gly	Thr 135	Pro	Glu	Arg	Asn	Thr 140	Val	Cys	Lys	Lys
Cys 145	Pro	Asp	Gly	Phe	Phe 150	Ser	Gly	Glu	Thr	Ser 155	Ser	Lys	Ala	Pro	Cys 160
Ile	Lys	His	Thr	Asn 165	Cys	Ser	Thr	Phe	Gly 170	Leu	Leu	Leu	Ile	Gln 175	Lys
Gly	Asn	Ala	Thr 180	His	Asp	Asn	Val	Cys 185	Ser	Gly	Asn	Arg	Glu 190	Ala	Thr
Gln	Lys	Cys 195	Gly	Ile	Asp	Val	Thr 200	Leu	Cys	Glu	Glu	Ala 205	Phe	Phe	Arg
Phe	Ala 210	Val	Pro	Thr	Lys	Ile 215	Ile	Pro	Asn	Trp	Leu 220	Ser	Val	Leu	Val
Asp 225	Ser	Leu	Pro	Gly	Thr 230	Lys	Val	Asn	Ala	Glu 235	Ser	Val	Glu	Arg	Ile 240
Lys	Arg	Arg	His	Ser 245	Ser	Gln	Glu	Gln	Thr 250	Phe	Gln	Leu	Leu	Lys 255	Leu
Trp	Lys	His	Gln 260	Asn	Arg	Asp	Gln	Glu 265	Met	Val	Lys	Lys	Ile 270	Ile	Gln
Asp	Ile	Asp 275	Leu	Cys	Glu	Ser	Ser 280	Val	Gln	Arg	His	Leu 285	Gly	His	Ser

FIGURE 2

Glu 1	Thr	Phe	Pro	Pro 5	Lys	Tyr	Leu	His	Tyr 10	Asp	Glu	Glu	Thr	Ser 15	His
Gln	Leu	Leu	Cys 20	Asp	Lys	Cys	Pro	Pro 25	Gly	Thr	Tyr	Leu	Lys 30	Gln	His
Cys	Thr	Ala 35	Lys	Trp	Lys	Thr	Val 40	Cys	Ala	Pro	Cys	Pro 45	Asp	His	Tyr
Tyr	Thr 50	Asp	Ser	Trp	His	Thr 55	Ser	Asp	Glu	Cys	Leu 60	Tyr	Cys	Ser	Pro
Val 65	Cys	Lys	Glu	Leu	Gln 70	Tyr	Val	Lys	Gln	Glu 75	Cys	Asn	Arg	Thr	His 80
Asn	Arg	Val	Cys	Glu 85	Cys	Lys	Glu	Gly	Arg 90	Tyr	Leu	Glu	Ile	Glu 95	Phe
Cys	Leu	Lys	His 100	Arg	Ser	Cys	Pro	Pro 105	Gly	Phe	Gly	Val	Val 110	Gln	Ala
Gly	Thr	Pro 115	Glu	Arg	Asn	Thr	Val 120	Cys	Lys	Arg	Cys	Pro 125	Asp	Gly	Phe
Phe	Ser 130	Asn	Glu	Thr	Ser	Ser 135	Lys	Ala	Pro	Cys	Arg 140	Lys	His	Thr	Asn
Cys 145	Ser	Val	Phe	Gly	Leu 150	Leu	Leu	Thr	Gln	Lys 155	Gly	Asn	Ala	Thr	His 160
Asp	Asn	Ile	Cys	Ser 165	Gly	Asn	Ser	Glu	Ser 170	Thr	Gln	Lys	Ala	Ala 175	Ala
Glu	Pro	Lys	Ser 180	Cys	Asp	Lys	Thr	His 185	Thr	Cys	Pro	Pro	Cys 190	Pro	Ala
Pro	Glu	Leu 195	Leu	Gly	Gly	Pro	Ser 200	Val	Phe	Leu	Phe	Pro 205	Pro	Lys	Pro
Lys	Asp 210	Thr	Leu	Met	Ile	Ser 215	Arg	Thr	Pro	Glu	Val 220	Thr	Cys	Val	Val
Val 225	Asp	Val	Ser	His	Glu 230	Asp	Pro	Glu	Val	Lys 235	Phe	Asn	Trp	Tyr	Val 240
Asp	Gly	Val	Glu	Val 245	His	Asn	Ala	Lys	Thr 250	Lys	Pro	Arg	Glu	Glu 255	Gln
Tyr	Asn	Ser	Thr 260	Tyr	Arg	Val	Val	Ser 265	Val	Leu	Thr	Val	Leu 270	His	Gln
Asp	Trp	Leu 275	Asn	Gly	Lys	Glu	Tyr 280	Lys	Cys	Lys	Val	Ser 285	Asn	Lys	Ala

FIGURE 3

Glu 1	Thr	Phe	Pro	Pro 5	Lys	Tyr	Leu	His	Tyr 10	Asp	Glu	Glu	Thr	Ser 15	His
Gln	Leu	Leu	Cys 20	Asp	Lys	Cys	Pro	Pro 25	Gly	Thr	Tyr	Leu	Lys 30	Gln	His
Cys	Thr	Ala 35	Lys	Trp	Lys	Thr	Val 40	Cys	Ala	Pro	Cys	Pro 45	Asp	His	Tyr
Tyr	Thr 50	Asp	Ser	Trp	His	Thr 55	Ser	Asp	Glu	Cys	Leu 60	Tyr	Cys	Ser	Pro
Val 65	Cys	Lys	Glu	Leu	Gln 70	Tyr	Val	Lys	Gln	Glu 75	Cys	Asn	Arg	Thr	His 80
Asn	Arg	Val	Cys	Glu 85	Cys	Lys	Glu	Gly	Arg 90	Tyr	Leu	Glu	Ile	Glu 95	Phe
Cys	Leu	Lys	His 100	Arg	Ser	Cys	Pro	Pro 105	Gly	Phe	Gly	Val	Val 110	Gln	Ala
Gly	Thr	Pro 115	Glu	Arg	Asn	Thr	Val 120	Cys	Lys	Arg	Cys	Pro 125	Asp	Gly	Phe
Phe	Ser 130	Asn	Glu	Thr	Ser	Ser 135	Lys	Ala	Pro	Cys	Arg 140	Lys	His	Thr	Asn
Cys 145	Ser	Val	Phe	Gly	Leu 150	Leu	Leu	Thr	Gln	Lys 155	Gly	Asn	Ala	Thr	His 160
Asp	Asn	Ile	Cys	Ser 165	Gly	Asn	Ser	Glu	Ser 170	Thr	Gln	Lys	Cys	Gly 175	Ile
Asp	Val	Thr	Ala 180	Ala	Ala	Glu	Pro	Lys 185	Ser	Cys	Asp	Lys	Thr 190	His	Thr
Cys	Pro	Pro 195	Cys	Pro	Ala	Pro	Glu 200	Leu	Leu	Gly	Gly	Pro 205	Ser	Val	Phe
Leu	Phe 210	Pro	Pro	Lys	Pro	Lys 215	Asp	Thr	Leu	Met	Ile 220	Ser	Arg	Thr	Pro
Glu 225	Val	Thr	Cys	Val	Val 230	Val	Asp	Val	Ser	His 235	Glu	Asp	Pro	Glu	Val 240
Lys	Phe	Asn	Trp	Tyr 245	Val	Asp	Gly	Val	Glu 250	Val	His	Asn	Ala	Lys 255	Thr
Lys	Pro	Arg	Glu 260	Glu	Gln	Tyr	Asn	Ser 265	Thr	Tyr	Arg	Val	Val 270	Ser	Val
Leu	Thr	Val 275	Leu	His	Gln	Asp	Trp 280	Leu	Asn	Gly	Lys	Glu 285	Tyr	Lys	Cys

FIGURE 4

Lys	Val	Ser	Asn	Lys	Ala	Leu	Pro	Ala	Pro	Ile	Glu	Lys	Thr	Ile	Ser
	290					295					300				
Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro
305					310					315					320
Ser	Arg	Asp	Glu	Leu	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys	Leu	Val
				325					330					335	
Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly
			340					345					350		
Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp
		355					360					365			
Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp
	370					375					380				
Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu	Ala	Leu	His
385					390					395					400
Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Pro	Gly			
				405					410						

Sequence: 290-410

FIGURE 4

Year	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100
1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100	

FIGURE 5

Glu 1	Thr	Phe	Pro	Pro 5	Lys	Tyr	Leu	His	Tyr 10	Asp	Glu	Glu	Thr	Ser 15	His
Gln	Leu	Leu	Cys 20	Asp	Lys	Cys	Pro	Pro 25	Gly	Thr	Tyr	Leu	Lys 30	Gln	His
Cys	Thr	Ala 35	Lys	Trp	Lys	Thr	Val 40	Cys	Ala	Pro	Cys	Pro 45	Asp	His	Tyr
Tyr	Thr 50	Asp	Ser	Trp	His	Thr 55	Ser	Asp	Glu	Cys	Leu 60	Tyr	Cys	Ser	Pro
Val 65	Cys	Lys	Glu	Leu	Gln 70	Tyr	Val	Lys	Gln	Glu 75	Cys	Asn	Arg	Thr	His 80
Asn	Arg	Val	Cys	Glu 85	Cys	Lys	Glu	Gly	Arg 90	Tyr	Leu	Glu	Ile	Glu 95	Phe
Cys	Leu	Lys	His 100	Arg	Ser	Cys	Pro	Pro 105	Gly	Phe	Gly	Val	Val 110	Gln	Ala
Gly	Thr	Pro 115	Glu	Arg	Asn	Thr	Val 120	Cys	Lys	Arg	Cys	Pro 125	Asp	Gly	Phe
Phe	Ser 130	Asn	Glu	Thr	Ser	Ser 135	Lys	Ala	Pro	Cys	Arg 140	Lys	His	Thr	Asn
Cys 145	Ser	Val	Phe	Gly	Leu 150	Leu	Leu	Thr	Gln	Lys 155	Gly	Asn	Ala	Thr	His 160
Asp	Asn	Ile	Cys	Ser 165	Gly	Asn	Ser	Glu	Ser 170	Thr	Gln	Lys	Cys	Gly 175	Ile
Asp	Val	Thr	Val 180	Asp	Lys	Thr	His	Thr 185	Cys	Pro	Pro	Cys	Pro 190	Ala	Pro
Glu	Leu	Leu 195	Gly	Gly	Pro	Ser	Val 200	Phe	Leu	Phe	Pro	Pro 205	Lys	Pro	Lys
Asp	Thr 210	Leu	Met	Ile	Ser	Arg 215	Thr	Pro	Glu	Val	Thr 220	Cys	Val	Val	Val
Asp 225	Val	Ser	His	Glu	Asp 230	Pro	Glu	Val	Lys	Phe 235	Asn	Trp	Tyr	Val	Asp 240
Gly	Val	Glu	Val	His 245	Asn	Ala	Lys	Thr	Lys 250	Pro	Arg	Glu	Glu	Gln 255	Tyr
Asn	Ser	Thr	Tyr 260	Arg	Val	Val	Ser	Val 265	Leu	Thr	Val	Leu	His 270	Gln	Asp
Trp	Leu	Asn 275	Gly	Lys	Glu	Tyr	Lys 280	Cys	Lys	Val	Ser	Asn 285	Lys	Ala	Leu

FIGURE 6

Glu	Thr	Phe	Pro	Pro	Lys	Tyr	Leu	His	Tyr	Asp	Glu	Glu	Thr	Ser	His
1				5					10					15	
Gln	Leu	Leu	Cys	Asp	Lys	Cys	Pro	Pro	Gly	Thr	Tyr	Leu	Lys	Gln	His
			20					25					30		
Cys	Thr	Ala	Lys	Trp	Lys	Thr	Val	Cys	Ala	Pro	Cys	Pro	Asp	His	Tyr
		35					40					45			
Tyr	Thr	Asp	Ser	Trp	His	Thr	Ser	Asp	Glu	Cys	Leu	Tyr	Cys	Ser	Pro
	50					55					60				
Val	Cys	Lys	Glu	Leu	Gln	Tyr	Val	Lys	Gln	Glu	Cys	Asn	Arg	Thr	His
65					70					75					80
Asn	Arg	Val	Cys	Glu	Cys	Lys	Glu	Gly	Arg	Tyr	Leu	Glu	Ile	Glu	Phe
				85					90					95	
Cys	Leu	Lys	His	Arg	Ser	Cys	Pro	Pro	Gly	Phe	Gly	Val	Val	Gln	Ala
			100					105					110		
Gly	Thr	Pro	Glu	Arg	Asn	Thr	Val	Cys	Lys	Arg	Cys	Pro	Asp	Gly	Phe
		115					120					125			
Phe	Ser	Asn	Glu	Thr	Ser	Ser	Lys	Ala	Pro	Cys	Arg	Lys	His	Thr	Asn
	130					135					140				
Cys	Ser	Val	Phe	Gly	Leu	Leu	Leu	Thr	Gln	Lys	Gly	Asn	Ala	Thr	His
145					150					155					160
Asp	Asn	Ile	Cys	Ser	Gly	Asn	Ser	Glu	Ser	Thr	Gln	Lys	Ser	Gly	Gly
				165					170					175	
Gly	Gly	Gly	Gly	Gly	Gly	Thr	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu
			180					185					190		
Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr
		195					200					205			
Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val
	210					215					220				
Ser	His	Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val
225					230					235					240
Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser
				245					250					255	
Thr	Tyr	Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu
			260					265					270		
Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Ala	Leu	Pro	Ala
		275					280					285			

FIGURE 7

[illegible]

FIGURE 7

Met	Asp	Lys	Thr	His	Thr	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu	Leu
1				5					10					15	
Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu
			20					25					30		
Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser
		35					40					45			
His	Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu
	50					55					60				
Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser	Thr
65					70					75					80
Tyr	Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn
				85					90					95	
Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Ala	Leu	Pro	Ala	Pro
			100					105					110		
Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln
		115					120					125			
Val	Tyr	Thr	Leu	Pro	Pro	Ser	Arg	Asp	Glu	Leu	Thr	Lys	Asn	Gln	Val
	130					135					140				
Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val
145					150					155					160
Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro
				165					170					175	
Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr
			180					185					190		
Val	Asp	Lys	Ser	Arg	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val
		195					200					205			
Met	His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu
	210					215					220				
Ser	Pro	Gly	Lys	Glu	Thr	Phe	Pro	Pro	Lys	Tyr	Leu	His	Tyr	Asp	Glu
225					230					235					240
Glu	Thr	Ser	His	Gln	Leu	Leu	Cys	Asp	Lys	Cys	Pro	Pro	Gly	Thr	Tyr
				245					250					255	
Leu	Lys	Gln	His	Cys	Thr	Ala	Lys	Trp	Lys	Thr	Val	Cys	Ala	Pro	Cys
			260					265					270		
Pro	Asp	His	Tyr	Tyr	Thr	Asp	Ser	Trp	His	Thr	Ser	Asp	Glu	Cys	Leu
		275					280					285			

FIGURE 8

[illegible]

FIGURE 8

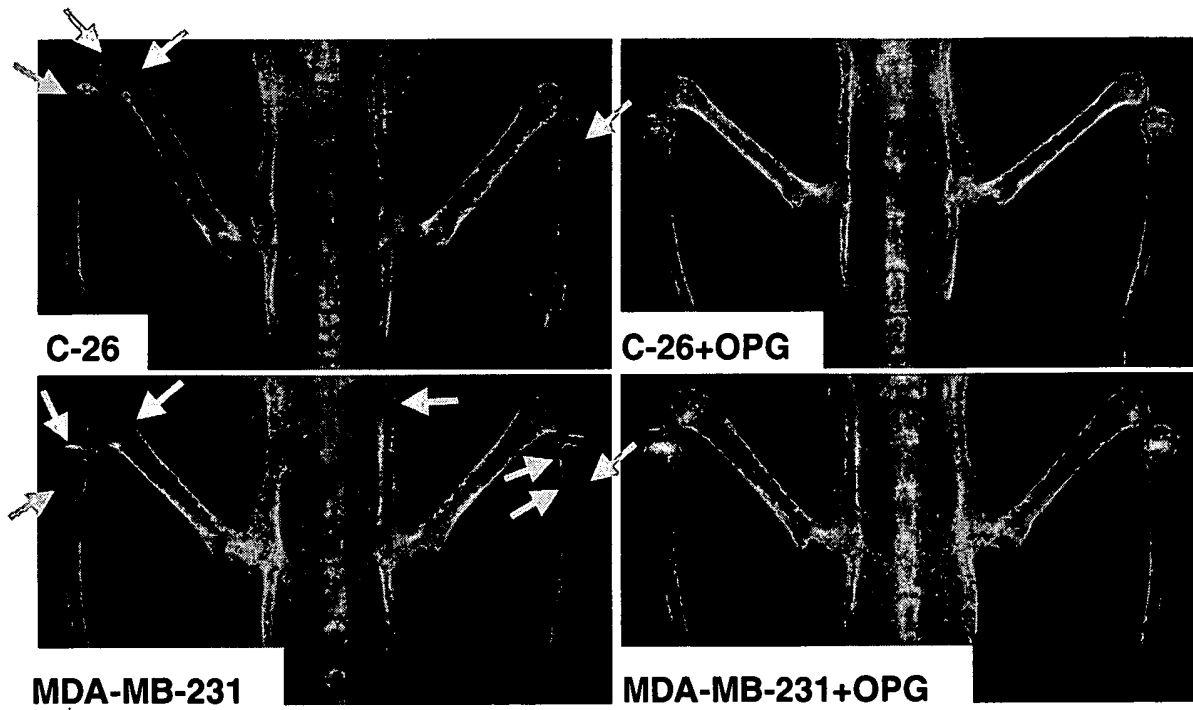


FIGURE 9

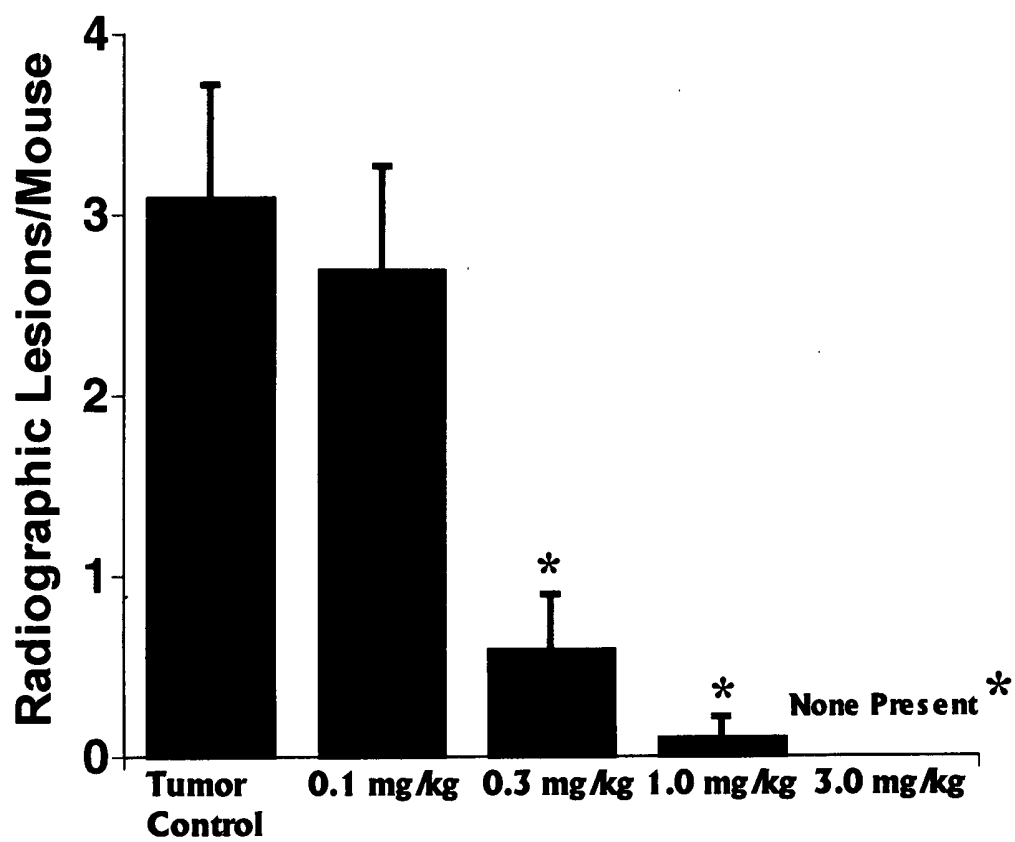


FIGURE 10

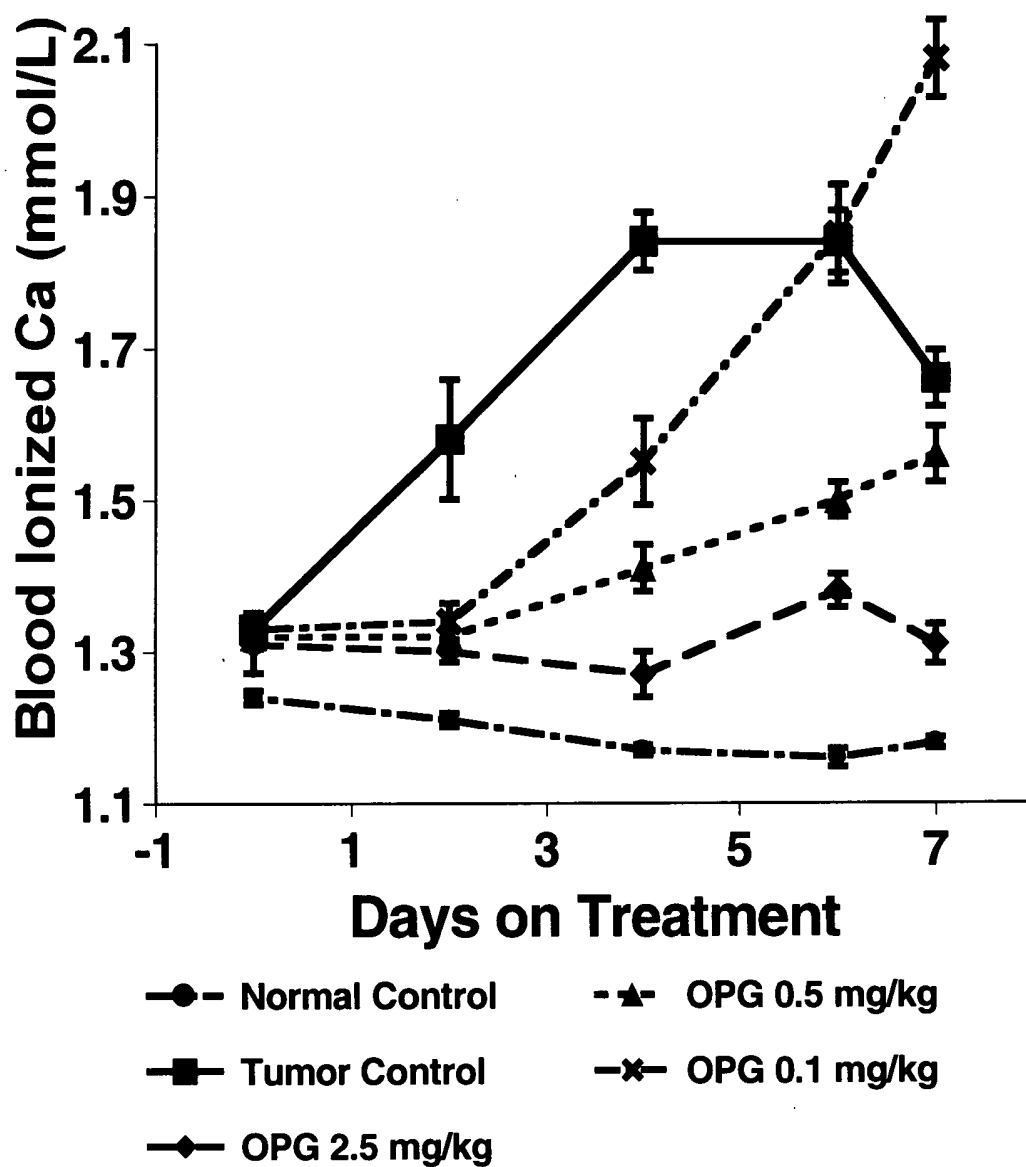


FIGURE 11A

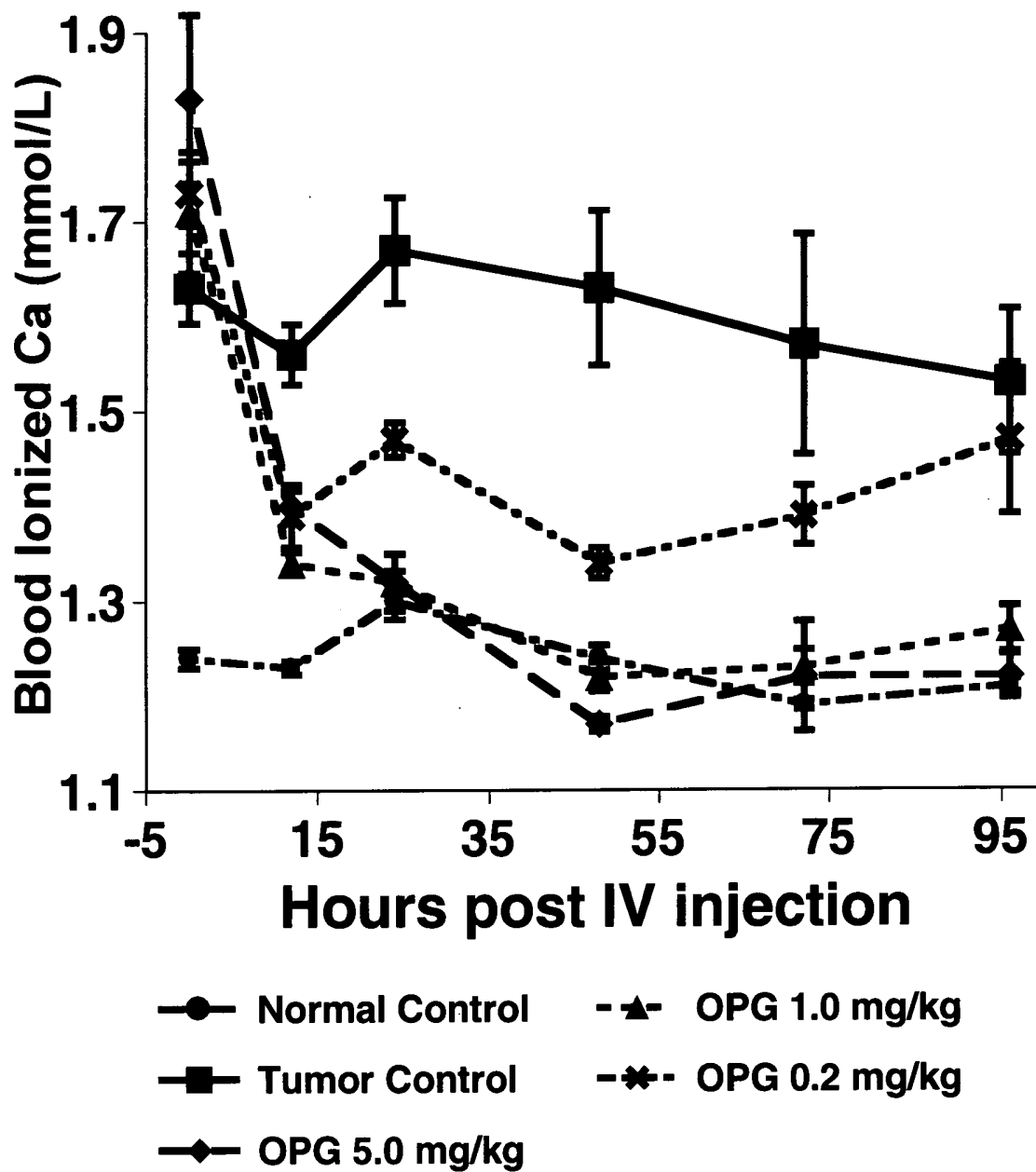


FIGURE 11B